

distorted by the tidal influence of the satellite. The linear diameters of primary and satellite are in a ratio of about 4 : 1.

The points of bifurcation on the Poincaré series are not investigated. Since the Jacobian ellipse determined by equation (iv) is known to be stable, there is ground for supposing that the series remains stable up to the point of separation. It therefore appears probable that the primary moves through a cycle of configurations in which Jacobi's and Poincaré's figures alternate. The angular momentum is decreased by about 30 per cent., at the ejection of each satellite.

"On the Action of the Spurge (*Euphorbia hiberna*, L.) on Salmonoid Fishes."\* By H. M. KYLE, M.A., D.Sc., St. Andrews University. Communicated by Professor McINTOSH, F.R.S. Received June 25,—Read December 12, 1901.

### *Introduction.*

It has been known for some years that the Irish peasantry employed a simple method of procuring salmon and trout through the agency of the Spurge (*E. hiberna*, L.). The plant cut into small pieces and pounded with stones, or simply trampled upon at some convenient spot on a river, forms an emulsion in the water which, being swept downward into the pools, carries death to all fishes in its course. The fatality thus produced seems to have been enormous—80 to 100 salmon are reported to have been killed at one time,† and again in the Bandon rivers 500 to 1000 fish of various descriptions are said to have been poisoned during one season.‡ In the light of the experiments to be recorded presently, these statements do not seem exaggerated, for the Spurge-extract, even in small quantities, is almost as fatal to fishes as corrosive sublimate.

The fatal effect of the Spurge on fishes has been known in other countries besides Ireland, but to what ingredient or ingredients of the plant these effects are due seems never to have been investigated. The following pages contain a brief record of experiments which, though incomplete in many ways, throw considerable light upon the action of the Spurge, and open out to view some interesting problems.

As the range of this research has included within its scope several

\* The Fishmongers' Company generously gave a sum for the carrying out of this research. Special thanks are also due to the Hon. G. W. Hely Hutchison, secretary to the Irish Inland Fisheries Commission, who forwarded plants of Spurge from Ireland.

† 'Report of the Inspectors of Irish Fisheries,' 1898, p. 193.

‡ *Ibid.*, 1892, p. 53.

branches of science, I have been obliged to seek assistance from specialists in the different departments, and I wish to acknowledge my indebtedness. Mr. Robertson, Lecturer in Botany at St. Andrews University, has aided me with the botanical literature on the subject, and the keen interest he took in the progress of the research was displayed in many valuable suggestions. To Dr. Fraser Harris, Lecturer in Physiology at the same University, I am even more indebted, since he freely gave his advice as to the best methods of conducting the physiological experiments which the research necessitated, and very kindly revised the manuscript. My indebtedness to the chemists will be displayed later, but I must here thank Professor McIntosh, F.R.S., for his kindly encouragement and the facilities he gave me for my work at the Gatty Marine Laboratory.

*Description of the Plant and its Chemical Composition.*

*Euphorbia hiberna*, L., or the Irish Spurge, is a member of the large order Euphorbiaceæ, which gives to medicine such well-known drugs and poisons as croton oil, cascarilla, and castor oil. It is a hardy perennial weed, growing to the height of about 2 feet, with dull greenish leaves and inflorescences of an orange-yellow colour. Its area of distribution is mostly on the Continent in France, Switzerland, and Italy, but it is also found in the South of England and South of Ireland. Its reputation is well known, for in all reference works, botanical or pharmacological, where it is mentioned, one finds the statement that it is used in Ireland to poison fishes.

The fresh plant is almost odourless, but the expressed juice from the laticiferous vessels and the emulsion formed in water have a very faint, pungent, and slightly aromatic odour. In this respect it differs somewhat from the officinal *Euphorbia* (*E. resinifera*, Berg), a native of Northern Africa, which is said to have a powerfully irritating acrid odour. In the latter, according to Flückiger,\* who examined the dried exported drug, this acidity is due to amorphous indifferent resin. It is probable that the fresh extract—with which alone we are concerned in *E. hiberna*—would differ somewhat from the analysis given by him. Thus he found no volatile oil on distilling the drug with water, whereas a small quantity of some volatile substance was obtained from *E. hiberna* by the same means. Again, he declares that no emulsion is formed in water by the drug obtained from *E. resinifera*. On the other hand, an emulsion characterises the fresh aqueous extract of *E. hiberna*. Flückiger's analysis would seem, therefore, to apply to the oxidation-products of the original substances in *E. resinifera*, and is hardly comparable with that of *E. hiberna* to be presently given.

In one respect *E. resinifera* differs essentially from *E. hiberna*: in the

\* 'Pharmacognosie des Pflanzenreiches,' p. 194; 'Pharmacographia,' p. 504.

analysis of the former given by Flückiger no mention is made of tannic acid, which in the latter is present in considerable quantity. This constituent has, however, been found in other species of Euphorbiaceæ—e.g., *E. lathyris*, L.,\* a native of Southern Europe but naturalised in England and Scotland. The following preliminary chemical examination of the Spurge was made by G. D. Lander, D.Sc., late of St. Andrews University :—

“The root-bark and stem contain a milky latex of acid reaction. The root-bark is particularly rich in latex. On standing, the expressed latex speedily solidifies to a gum-resin.

“Cold water forms a light-brown emulsion of characteristic odour. On boiling the bark with water, a more concentrated extract, darker in colour, may be got. A small quantity of a solid volatile with steam was separated. This appears to be the odoriferous body. The liquid condensed from the boiling water is neutral, indicating the absence of volatile organic acids or alkaloids. No indication of the presence of alkaloids could be got in a hydrochloric acid extract. On distilling with alkali, an alkaline distillate is obtained, but this is probably due to ammonia.

“The liquid obtained by extraction of the root-bark with hot water was an acid emulsion of resin, in a solution containing starch, and probably also dextrin and gum. Much resin is left unemulsified in the bark when the extraction is effected by hot water.

“The concentrated extract gave a copious precipitate when mixed with 10 volumes of absolute alcohol. This precipitate indicates the presence in the extract of dissolved starch, and possibly also dextrin and gum, which are probably innocuous. The alcoholic solution contains resin associated with some gum. The water extract of stem and leaves possessed the same properties.”

Inasmuch as it was found by experiments on trout that the volatile substance could not account for the fatal action of the Spurge, but that the acid emulsion of resin did, Dr. Lander prepared a quantity of this by the alcoholic method, carefully removing the alcohol by evaporation after the emulsion had been formed. This emulsion so prepared had precisely the same fatal effects on trout as the freshly prepared aqueous extract of the Spurge.

Indications were obtained, however, at a later stage of the work, that the Spurge-extract might still further be resolved into its components, and the following examination was thereupon carried out at the physiological laboratory.

The emulsion formed by cold water is of a dirty-grey or light-brown colour, with a small quantity of a powdery solid in suspension. By repeated filtration this emulsion is broken up, and a clear brownish solution is obtained. If the emulsion is retained in a tightly stop-

\* Hooker, ‘Flora’ (1870), p. 329.

pered bottle, it remains unchanged for many days, but if left open to the air even for a few hours, rapid changes take place. A brownish flocculent precipitate gradually takes the place of the greyish emulsion, and remains suspended for some time in the solution, which is now becoming of a dark brown colour. If this solution is filtered, and the filtrate again allowed to stand in the air, a precipitate again forms similar to the previous one, and this process may go on for weeks.

It is obviously impossible to perform satisfactory tests upon the original emulsion, and on the other hand examination of the filtrates cannot be expected to give exact information with regard to the original extract. Such an examination seemed necessary, however, because the results obtained would throw light upon the changes the extract had undergone, and reasoning from these results, the alterations which the Spurge-extract undergoes when thrown into the rivers in Ireland, might be followed.

A minute quantity of proteid material was detected by means of the xanthoproteic, Millon's, and other tests. The presence of this proteid interfered with the reactions given by other constituents of the extract, but otherwise it is of no importance. Starch granules were readily identified by means of iodine in the precipitate which forms in the extract on standing. Glucose was identified by means of the phenylhydrazin test, and was present in considerable quantity.

Tannin, or some ally of tannic acid, was identified by the precipitates given by the salts of iron and copper, as well as by various other reagents. Solutions of tannic and gallic acids were then prepared in varying proportions, and it was found that solutions of approximately 1 per cent. gave reactions similar (as to colour, quantity, and rapidity of appearance of the precipitates) to those given by the aqueous Spurge-extract. As the strength of the extract was about 1 gramme of plant to 1 c.c. of water, it follows that the plant contains at least 1 per cent. of tannic acid. The percentage is probably greater than this, because much tannin remains in the tissues of the plant after the first filtrate is removed, and also because the presence of the proteid material inhibits somewhat the reactions given by tannic acid.

The constituents of the aqueous Spurge-extract would thus seem to be: 1, proteid; 2, starch; 3, glucose; 4, resin and gum; 5, tannic acid; 6, volatile substance.

The metals calcium, sodium, and potassium are also present, but in what form was not determined. It is worthy of special notice that no alkaloid was found in the latex. If the analysis just given be compared with those worked out by botanists for other species of the *Euphorbiaceæ*, it will be found that *E. lathyris*\* comes nearest to *E. hiberna*.

\* De Bary, 'Comparative Anatomy of the Phanerogams and Ferns,' English translation, 1884, p. 184.

In *E. lathyris* as well as in other species of the Euphorbiaceæ, malic acid in the form of its calcium and other salts occurs in abundance, and it is possibly present in *E. hiberna*. If present in the acid form in the extract, it would account for some of the changes that occur when the extract is exposed to air, but otherwise it is of little importance.

In his description of *E. resinifera*, Flückiger mentions the presence of a compound which he calls Euphorbon, with the composition  $C_{15}H_{24}O$  or  $C_{20}H_{36}O$ . Whether this substance, probably an oxidation product, or any similar substance, is present in *E. hiberna* was not determined, and it is due in part to the incompleteness of the chemical analysis of the plant, that certain discrepancies to be shown hereafter can not be fully explained.

It is necessary to mention the various extracts of the Spurge that were employed, and the methods by which they were prepared. What will be referred to as the "fresh extract" means an aqueous extract which has been prepared by washing and chopping up the stems, roots, and leaves of the plant, and allowing them to stand in water within a closed vessel. The vessel was shaken well several times, and at the end of 2 hours the liquid was poured off, filtered once, and measured. The aim of this method was to obtain an extract resembling as nearly as possible that which is employed in Ireland in poisoning the rivers, and was decided upon after various trials. It was found that if more than 2 hours were given to the formation of the extract the emulsion tended to break up and disappear. If the chopped-up plant was left for 24 hours in water the emulsion still persisted, but was not so thick and disappeared on once filtering, whereas on standing for 2 hours only, the emulsion passed through the filter and remained in the filtrate. The reason for filtering at all was to get rid of a large amount of woody and insoluble material which could play little or no part in the action of the Spurge on fishes, but made the liquid turbid and obscure.

Whether the emulsion was present or absent, and whether the liquid was poured off from the plant at the end of  $\frac{1}{2}$  hour or 4 days, made no difference in the fatal effects which it had upon the trout. But it was found desirable to have some standard solution with which all other extracts and preparations could be compared. The standard was arrived at by comparing the amount of the liquid drawn off with the weight of the plant employed—1 c.c. of liquid to 1 gramme of plant being taken as the 100 per cent. extract. When percentages of the fresh extract are spoken of, therefore, they are calculated from this as the standard.

This is admittedly a rough measure and for two reasons. On the one hand, it does not express the percentages in terms of the active ingredient, which would have been very desirable indeed had it been possible. On the other hand, the short space of 2 hours during which the plant is macerated, does not by any means exhaust the active

ingredients of the plant. The process of maceration may be repeated on the same plant three or four times, and the resulting liquids will still be as fatal or almost as fatal in their action on the trout as the first. This, although it does not do away with the value of the standard chosen, shows that the active ingredient or ingredients are present in the plant in larger quantity than is represented by the standard fresh extract. Further it shows that the deadliness of the plant, when placed in the Irish rivers, is not a matter of a few minutes only, but of many hours and even days.

The fresh extract prepared as described has all the characteristics which have been already given. In addition, however, it is highly oxidisable, as its power of rapidly decolourising potassium permanganate shows. It should be mentioned also that the composition of the plant may vary throughout the year, and that the above examinations were made in May and June. The changes which the extract undergoes on exposure to air, as well as the initial composition of the plant and its change during the year, demand more thorough determination ere a complete explanation can be given of all the effects the plant-extract produces. Here it is only possible to account for a few, but perhaps the most important phenomena.

#### *Action of the Fresh Spurge-extract and Latex.*

When rubbed on the skin, no sensation is noticeable, but the surface becomes dry and rough. Later, the part becomes slightly flushed. When taken by the mouth in small quantities it has a nauseous, disagreeable taste. At the back of the tongue and in the gullet it produces an irritant, burning sensation, which remains for several hours. Salivation, if any, is very slight. In the stomach it has little effect. At first there is a slight tendency to nausea, but this soon passes away and no ill-effects of any kind ensue.

The solution which has stood for some time and been repeatedly filtered, loses this effect. It is still slightly acid, and leaves a soft, soapy sensation on the back of the tongue, whilst in the stomach it has no effect whatsoever.

It is said that the salmon which are killed by the Spurge-extract in the Irish rivers are used as food without any ill-effects resulting. In order to test this point, a stray kitten which had wandered into the Gatty Laboratory was permitted to feed upon the poisoned trout. When no signs of poisoning were shown, the emulsion obtained from the extract after removal of the volatile substance, was placed in its milk—about a quarter being emulsion. This diet was continued for 4 days, at the end of which time the kitten appeared in good condition and health, and its appetite for the poisoned trout and milk had in no way diminished. But not only has the Spurge-extract little

or no effect on the intestinal canal of the higher animals, it has also none on that of the fishes, as the following experiment showed. Several trout were set apart in a separate tank by themselves and fed for 6 weeks on boiled mussels, which had been steeped for some time in the Spurge-extract. The extract employed was the ordinary aqueous preparation, containing therefore a certain amount of the volatile substance, and fatal to the trout when immersed bodily into a small proportion of it in water. Yet when taken into the alimentary canal, through the mussel as medium, it had no apparent effect—the trout living upon the food appeared as active and as healthy at the end of 6 weeks as those in the neighbouring tank, which had been fed upon the ordinary boiled mussel. There could be no doubt that the fish really absorbed some of the extract, because the mussels were so thoroughly steeped in the extract that some of it must have remained unchanged in their tissues; and again the trout were kept in a half-starved condition, so that when fed they eagerly grabbed the mussel before it had been more than a second or two in the water. There was no time therefore for the extract to diffuse out into the water, and it must consequently have been ingested.

Not only does the aqueous extract of the Spurge—with which we are mostly concerned—seem to have no action on the alimentary canal in moderate quantities, it also seems incapable of being absorbed from the skin, or if absorbed is not fatal. Several toads which were immersed for 7 days in an aqueous extract, but so that their heads and necks were above the surface and the animals were thus able to breathe freely, were alive at the end of that time and able to respond to stimuli. This extract had been freshly prepared, and produced certain characteristic effects on the vascular system to be presently described. What happened in the case of the toads can readily be inferred from the known action of tannic acid. The peripheral circulation would be affected, and the skin might indeed be “tanned” to a certain extent, but this would protect the internal organs from harm, and evidently did so whilst the toads were immersed in the solution.

From the foregoing series of observations, it might be inferred that the action of the aqueous Spurge-extract is mainly local, and the following experiments seem to decide conclusively in favour of this inference. The gastrocnemius muscle of pithed frogs gave the normal responses to stimuli, both when irrigated directly by the extract and when the latter had been previously injected into the lymph. The heart of a pithed toad when irrigated by the extract, as well as after injection into the lymph, varied as little from its normal beating as it did when irrigated by normal saline solution. These experiments were performed both with the fresh extract and with the extract some days old, and it may clearly be inferred that the aqueous Spurge-

extract has no action on muscular tissue when treated in the above way. Injection of the extract into the muscle was not attempted.

Although both the motor nervous and muscular systems are not affected, the same cannot be said for the sensory nervous system. Very few experiments were made on this point, but they seem sufficient to show that the sensory nerve-tracts are slightly paralysed at some part of their course. The reflex time of two pithed frogs, which were allowed to remain in this condition for some hours after the operation to allow them to recover from the shock, was found to be several seconds greater on the average after injection of the Spurge-extract than before. And again, two similarly treated frogs responded to weaker electrical stimuli before injection of the extract than after. Taken in conjunction with the previous experiments on the motor system, these results show that the sensory nerves or central nervous system are in some way affected.

The quantity of volatile substance which is present in the fresh aqueous extract, though it produces a slight paralysis of sensation, is not sufficient to account for the fatal effects which the same extract has on fishes, and also on frogs when treated in a certain manner.

If a pithed frog's lung be dissected out and irrigated with normal saline solution, the circulation in the capillaries may be watched for a long time. When now a few drops of the Spurge-extract are placed on the lung, a great and almost immediate change is seen. The capillaries shrink visibly, the blood corpuscles are pressed backwards into the arterioles and sway to and fro with each beat of the heart. The heart-beats become slower and more protracted if the Spurge irrigation is continued. The whole lung contracts to half its previous size, and in the larger vessels which also contract, a condition of stasis sets in, ending with the death of the frog within half an hour of the operation. If the mesentery, and not the lung, be chosen for examination, a similar result is obtained, but this has the additional advantage of showing that the action is quite local. If a small portion of the intestine is irrigated with the extract, the blood ceases to flow in the arteries leading to that part, but not in the neighbouring ones.

The effects here described are obviously due to the tannic acid, and the application of the latter directly produces the same result. Even a weak solution, 0.01 per cent. of tannic acid (1 in 10,000), has a marked effect upon the capillaries, whilst a 1 per cent. causes stasis almost immediately. Further, when the lung is irrigated with normal saline solution after treatment with 0.01 per cent. of tannic acid, circulation is gradually re-established, but not so after 1 per cent. The latter case resembles that of the Spurge-extract, for irrigation with normal saline solution after treatment with the fresh extract enables the circulation to be maintained in the vessels which had not become constricted, but cannot revive it in the others.



Table I.—Summary of Experiments which were made in order to discover the Action of the Spurge-extract on Fishes and other Animals.

Strength and nature of solution.	Period within which it is fatal.	Animal experimented on.	Mode of application.	Notes.
20 per cent. of "fresh extract" (=0·2 per cent. of tannin approx.)	5 minutes	Trout	Animals immersed in solution	Control experiments performed at same time. Other trout immersed in fresh water in vessel of similar form. The variation in length of period which proved fatal was considerable.
5 per cent. of do.	10 to 30 minutes	Do.	Do.	This probably arose from the condition of the animals when experimented on.
4 per cent. of do.	10 to 30 minutes	Do.	Do.	The symptoms were the same in both strong and weak solutions. In 50 per cent. of cases great excitement shown—the fish darting about wildly for some time, then resting exhausted, frequently in an inverted position. Rate of breathing increased from 120 to 130 per minute—the rate in control specimen—to 140 to 160 per minute. In 50 per cent. of cases no excitement, and animal remained in normal position. Gulp- ing movement of jaws at intervals of 5 to 10 res- piratory movements, accompanied by jerking movements of body. Later, rate of breathing became gradually slower.
1 per cent. of do.	$\frac{3}{4}$ and $1\frac{1}{2}$ hours	Do.	Do.	Loss of sensibility then displayed. Gill-covers held apart from pectoral arch so that gills could be seen during inspira- tion.
0·2 per cent. of do.	1 to 2 hours	Do.	Do.	
0·1 per cent. of do.	$1\frac{1}{2}$ to 2 hours	Do.	Do.	
0·1 per cent. of do. after standing for 6 days	2 to 4 hours	Do.	Do.	
0·05 per cent. of do.	4 to 6 hours	Do.	Do.	
0·01 per cent. of do.	4 to 6 hours	Do.	Do.	
0·2 per cent. of "fresh ex- tract" formed from fruit and leaves	$2\frac{1}{2}$ to 4 hours	Do.	Do.	Roots seem to have more of poisonous ingredients, but these experiments were performed early in September, when stem and leaves begin to lose their sap.

Strength and nature of solution.	Period within which it is fatal.	Animal experimented on.	Mode of application.	Notes.
0.2 per cent. of "fresh extract" from stem and leaves	2 to 4 hours	Trout	Animals immersed in solution	
0.2 per cent. of "fresh extract" from roots	1 to 3 hours	Do.	Do.	
0.2 per cent. of emulsion minus volatile solid	40 minutes to 1 hour	Do.	Do.	The emulsion prepared in this way is stronger than the fresh extract. Thus 0.2 per cent. of this is equivalent to about 0.5 per cent. of fresh extract.
0.2 per cent. of emulsion minus volatile solid. 4 weeks later	1 to 2 hours	Do.	Do.	
Solution of volatile solid		Do.	Do.	Death did not result, although animals displayed excitement. Perhaps quantity too small.
1 per cent. of "fresh extract" of Spurge		Gastrocnemius of pithed frogs	Direct irrigation	No effect produced. The responses given did not differ from those of normal frog.
100 per cent. of do.		Do.	Do.	
100 per cent. of do.		Do.	Injected into lymph space	
100 per cent. of do.		Heart of pithed toads	Direct irrigation, and injection	No effect produced. Heart's action remained normal.
100 per cent. of do.	..	Lung of pithed frog	Direct irrigation	The lung contracted visibly. The capillaries were constricted and a condition of stasis set up in larger vessels, all within a few minutes.
20 per cent. of do.	..	Do.	Do.	
0.1 per cent. of tannic acid	..	Do.	Do.	The effect produced was precisely similar to that described as due to the Spurge-extract, the stronger solutions being more rapid in their action.
1 per cent. of do.	..	Do.	Do.	

Strength and nature of solution.	Period within which it is fatal.	Animal experimented on.	Mode of application.	Notes.
100 per cent. of "fresh extract."	..	Pithed frog's mesentery	Direct irrigation	Effect as on lung, but seen to be local. Circulation was maintained in neighbouring vessels not affected by the extract.
20 per cent. of do.	..	Do.		
2 per cent. of do. (approx.)		Frog	Immersed in solution, but so that head was free	Lived thus for 7 days.
Do.	..	Frog pithed	Injection	Reflex time for response to stimuli taken before and after injection, greater in latter case.
2 per cent. of do. (approx.)	..	Frog pithed	Injection	A stronger electrical stimulus required to obtain a response, under the influence of the Spurge-extract " than under normal conditions.
0.01 per cent. tannic acid	5 to 6 hours	Trout	Immersed in solution	Fish quiescent, no paralysis apparent, breathing irregular after some time, gill-covers a little strained but not greatly.
0.02 per cent. tannic acid	2½ hours	Do.	Do.	<i>Post-mortem</i> examination showed that great sloughing of the epithelium of the gills had taken place, more especially in the stronger solution.
Finely powdered starch in state of suspension in water	..	Do.	Do.	Animal immersed for 5 hours without showing any signs of discomfort. Animal took food in solution. A fine powder, therefore, is not harmful in itself.
Emulsion of resin and mucilage in water	..	Do.	Do.	No effect.
0.01 per cent. tannic acid and starch and aleurone	2½ hours	Do.	Do.	Rapidity of action apparently increased.
0.5 c.c. of "fresh extract"	12 hours	Do.	Injected into abdomen	The first specimen injected was much larger than other two — the third small and thin. Symptoms similar. At first no signs of change.

Strength and nature of solution.	Period within which it is fatal.	Animal experimented on.	Mode of application.	Notes.
0·4 c.c. of do.	6 hours	Trout	Injected into abdomen	<p>After 2 hours diminished sensibility shown, but this passed off later. Breathing heavy and deep with gulping movements of jaws intermittently. In 2nd and 3rd colour became very dark, with the red spots more conspicuous; for <i>post-mortem</i> examination, <i>vide</i> p. 63.</p> <p>Weak solutions of Spurge and tannin had little apparent effect upon early stages of trout. The circulation was hardly affected. In later stages stasis was shown in the capillaries at tip of notochord and in pseudo-branch of gill-cover. Over yolk-sac and body, however, circulation maintained. This both in Spurge solution and in tannic acid.</p> <p>Heart-beats increased from 50 to 60 when at rest and 80 to 85 when active to 90 to 110 per minute. Later frequency fell to 80, and then became gradually slower until death occurred. Gulping movements of the jaws frequent, synchronous, or almost so, with failure of ventricular beat. Heart continued to beat feebly for some minutes after circulation in body had ceased.</p>
0·3 c.c. of do.	3½ hours	Do.	Do.	
10 per cent. of do.	2 hours	Trout post-larval	Animal immersed in solution	
10 per cent. of do.	1 hour	Do. later stage	Do.	
0·01 per cent. tannic acid		Do.	Do.	
0·1 per cent. tannic acid	1 hour	Trout, post-larval (later stage)	Animal immersed in solution	

If we turn now to the action of the Spurge on fishes, we shall find that the theory which has accounted for its action on frogs renders it possible to understand a series of complex phenomena, which at first sight are very puzzling. Fishes, unlike frogs, are extremely "nervous" animals, and they display symptoms of fright or excitement, which must be carefully distinguished from those really due to the Spurge. The details of the experiments are given in the annexed

table. Here it is only necessary to give analysis of the symptoms and explain how they are caused.

One of the symptoms frequently displayed by the trout after immersion in a solution of the Spurge-extract is great excitement. The animals dash wildly about, and soon or late turn over on their backs, remaining thus for a long time if the solution is weak, until they die. Of twenty examples, ten displayed these phenomena, but the other ten showed no excitement, and remained in the normal position until within a few minutes of death. This variability was seen both in weak and strong solutions of the extract, and makes it impossible to believe that these symptoms are directly due to the Spurge. This negative conclusion is further strengthened by the fact that those fishes which possess air-bladders, and especially the trout, very readily lose their balance on seemingly slight provocation. Thus, if these trout are placed in water of higher temperature than they have been accustomed to, or even if exposed in a glass vessel to the rays of the sun—many of them will turn over on their backs and remain so until placed in colder water, or until they die. Sometimes, also, if suddenly startled, they display all the symptoms of excitement described above; and the only conclusion which can be drawn is, that the presence of anything unusual if sufficiently powerful, will induce a state of excitement in the trout leading to a loss, temporary or permanent, of the power of balancing themselves.

This loss of balance seems to arise from an affection of the central nervous system, causing an increased secretion of the gaseous contents of the air-bladder, at the same time having an inhibitory effect on the muscular tissue surrounding the opening of the air-bladder into the œsophagus, because it is invariably noticed in those trout which have a period of excitement and then come to rest, exhausted, yet remaining in the normal position, that successive bubbles of gas escape from their mouths, whereas no bubbles are to be seen in those cases where the trout loses its balance. Why this nervous affection should occur in some cases and not in others is as difficult to explain as the origin and variability of nervous diseases in general.

Another symptom of the same order is a peculiar gasping movement or spasm of the jaws and gill-covers, which is of constant occurrence and increases in frequency the longer the trout are immersed in the solution of the Spurge. But this phenomenon may appear under a variety of circumstances. Professor McIntosh noticed it whilst experimenting with various drugs upon young salmon, and he found that each spasm was accompanied by a discontinuity in the contractions of the ventricle. It may at times be noticed in the trout when under normal conditions, but occurs more frequently under abnormal conditions—as, for example, after the trout have been startled and excited in any way. It thus may be one of the

results of the nervous affection mentioned in the previous paragraph. Whilst these spasms therefore arise from the presence of the Spurge and may be called a secondary effect, they cannot be considered as characteristic of nor as directly due to its action.

Another symptom which observation, if confined to the action of the Spurge on trout, might lead one to think diagnostic, is the constant shedding of mucus from the mouth and skin. And one is the more ready to admit this, seeing that tannic acid, which has this effect, plays an important part in the action of the Spurge. But if trout are placed in clean water in a glass vessel immediately on capture, it will be noticed, after they have calmed down from their excited condition, that the water contains an abundant quantity of stringy mucous material. The shedding of mucus seems to occur very readily in salmonoid fishes, perhaps in all, and may be a symptom of the nervous excitement into which the animals are thrown. Again, the change that comes over the breathing may be due to the same cause. The frequency of this is increased during the first few minutes, but later falls below what it was to begin with. In the young post-larval trout, it was noticed that this occurred synchronously with a rise and fall of the pulse-frequency.

Only on two occasions was any sign given that the digestive system was interfered with. In these cases the trout, after being immersed for some time in a solution of the Spurge, vomited the contents of their stomachs. This again seems to arise from the derangement of the central nervous system already mentioned.

Excluding these cases there are still one or two symptoms which seem to display the direct local and distant effects of the Spurge, and though separately each may arise from other causes, yet taken together they seem to be characteristic of the action of the Spurge.

When the trout have been immersed for some time in the solution of the Spurge, it is noticeable that the gill-covers do not close completely over the gills, and that the latter can partly be seen even when the former should be quite closed. Further, the gills themselves appear swollen and of a brighter scarlet than under normal conditions. *Post-mortem* examination did not show any great difference from the normal. Sometimes a portion of the gill filaments would be injected with blood, showing that inflammation had been present there, but usually the naked-eye appearance was quite normal. In sections the poisoned specimens showed considerable disintegration of the mucus epithelium of the gills, rupture having apparently taken place in the underlying connective tissue, so that the capillaries which remained intact were left denuded. This was not present everywhere, but was nevertheless distinct from the normal condition. The capillaries also were much contracted and of smaller calibre than is usually the case. Further, though this difference from the normal

was not so distinct as the others, the larger blood-vessels were distended with red blood corpuscles.

Another symptom which is very apt to be overlooked, but which seems undoubtedly to be due to the Spurge, is a distinct loss of sensibility displayed by the trout after being immersed for some time in the solution of the extract. They become quiescent and sluggish, and whether lying on their backs or in the normal position permit themselves to be touched and moved about by the finger. This paralysis does not extend however to the motor system, because they are able to dart about in their accustomed manner if a sufficiently strong stimulus be given. Only two cases were noticed out of twenty in which the body was contorted and there seemed to be motor paralysis of one side. As death approached this sensory paralysis increased and it required still stronger stimuli to rouse the animal, but except in the two cases mentioned the motor system seemed fully capable of performing its functions until within a few minutes of death. If the solution of the Spurge is strong, death ensues so rapidly after immersion that it is somewhat difficult to detect these various stages, but they are easily followed when death does not take place for an hour or more, as in 0.1 per cent. solutions and under. This loss of sensibility is evidently similar to what occurs in the frogs, but in the trout it is more conspicuous.

Neither macroscopic nor microscopic investigation (the latter by sections) revealed any change in the tissues which could account for the fatal action of the Spurge. The alimentary canal (excluding the gills), the liver, spleen, and kidneys presented precisely the same appearances in the normal trout and in those killed by immersion in solutions of the Spurge. When the Spurge-extract was injected into the abdominal cavity, however, a distinct change was noticed in the vascular system of the alimentary canal. The methods employed for fixing and staining the tissues\* were the same in all cases, so that the change to be described could not arise in this way. The capillaries lying in the submucosa within the circular muscular layer of the stomach and intestines were found to be dilated and filled with red corpuscles, showing that congestion had occurred. In the normal trout, and in those killed by immersion bodily in the Spurge-extract, these blood-vessels appeared in section as small loose-walled capillaries containing but few corpuscles and often none at all. This change had evidently been produced by the tannic acid component of the Spurge, in the manner already mentioned when describing the action of the Spurge and tannic acid on the vascular system of the frog. The blood-

\* Fixation, by mixture containing gl. acetic acid (7 parts), 40 per cent. formaldehyde (3 parts), 70 per cent. alcohol (90 parts). This was found to give better results for epithelium than either corrosive sublimate or Flemming's solution. Staining, most usually by hæmalum and alcoholic eosin.

vessels of the kidney did not display this difference from the normal condition, which lends further proof of the quite local action of the component of the Spurge which has fatal effects, because the kidneys lie behind the air-bladder and are thus protected from whatsoever may be injected into the abdominal cavity, unless it reaches them by way of the circulation.

The time taken by the Spurge-extract to be fatal when injected into the abdominal cavity may be quoted here in order to show that the fatal effects of the Spurge in rivers arise from some action on the gills. An injection of 0.5 c.c. of fresh extract took more than 12 hours to be fatal. The same quantity in 500 c.c. of water would be fatal within less than 2 hours were the fish immersed in it, that is, if it acted on the gills. A stoppage in the gills affects the whole circulation, whereas in any other part the effect is local.

The experiments recorded in Table II give some notion of the deadly nature of the Spurge. Only in four cases out of many did the fish recover when removed from the Spurge solution to fresh water. In the first two cases the animals were immersed in strong solutions for a short time, too short apparently for the Spurge to have fatal effects, although the inertness of the fish when removed to fresh water showed that the poison had really affected their tissues. The other two cases show that the extract becomes somewhat less deadly after standing for several days, probably because a fungus gradually develops in it and thereby lessens the amount of tannic acid in the solution.

When the fish are immersed in solutions of pure tannic acid, the effects are similar to those produced by the Spurge-extract. The solutions employed were of 0.01 per cent. and 0.02 per cent. strength. In the former, death occurred within 4 hours, in the latter within 2 hours. There was no excitement on immersion, no loss of sensation, nor loss of balance. The gill-covers displayed spasmodic movements and were maintained wider open than in the normal trout, just as when the fish were under the action of the Spurge-extract. Also, when the trout were removed from the solution of tannic acid to fresh water they failed to recover. *Post-mortem* examination showed that the sloughing of the epithelial covering of the gills was more marked in the case of tannic acid, especially in a 1 per cent. solution, than in the case of the Spurge. A further difference was the absence of any sign that the nervous system was affected.

A comparison of the times which the tannic-acid solutions and the Spurge-extract solutions took to be fatal, given in Table I, shows that the latter is more rapidly fatal in its action than the supposed percentage of tannic acid it contains (1 to 2 per cent.) would allow one to expect. A 0.1 per cent. solution of the fresh extract of the Spurge is fatal in less than two hours, and this solution, according to the calcu-



lation, should contain about 0·001 per cent. of tannic acid. This latter quantity of tannic acid should therefore be fatal within 2 hours, whereas a solution ten times stronger took 4 hours, and one twenty times stronger just the same time, viz., 2 hours. After making due

Table II.—Experiments to Test the Power of Recovery which the Trout possessed after being immersed in various solutions for some time.

Strength and nature of solution.	Period within which it is fatal.	Duration of immersion.	Recovery, or lapse of time until death occurred.
20 per cent. of "fresh extract" (0·2 per cent. tannic acid, approx.)	5 minutes ..	3 minutes	Recovery.
5 per cent. of "fresh extract"	10 to 30 minutes	3 minutes	Recovery.
5 per cent. do. ....	10 to 30 minutes	15 minutes	Death within 20 minutes.
1 per cent. do. ....	1 to 1½ hours	1 hour ..	Death within ½ hour.
0·1 per cent. do., 4 days old	1½ to 2 hours	1¼ hours	Death within ½ hour.
0·1 per cent. do., 5 days old	1½ to 2 hours	1¼ hours	Death within ½ hour.
0·1 per cent. do., 6 days old	1½ to 4 hours	1¼ hours	Death within 1¼ hours.
0·1 per cent. do., 8 days old	1½ to 4 hours	¾ hour ..	Death within 3 hours.
0·1 per cent. do., 10 days old, and from which a precipitate had been filtered	..	2 hours ..	Recovery.
0·01 per cent. do. ....	4 to 6 hours	4 hours ..	Death within 10 minutes.
0·01 per cent. do. ....	4 to 6 hours	3½ hours	Death within 1½ hours.
0·01 per cent. of "fresh extract," 2 days old	..	4½ hours	Death within 1½ hours. One specimen recovered.
0·2 per cent. of emulsion minus volatile solid. (= 0·5 per cent. "fresh extract" approx.)	¾ hour	40 minutes	Death within 10 minutes.
As do., but 4 weeks later	1½ hours	1 hour	Death within ¾ hour.
0·01 per cent. of tannic acid	5 to 6 hours	4½ hours	Died 1 hour later.
200 per cent. of tannic acid.	2½ hours	2 hours	Died within 1 hour.

allowance for variability in specimens, it seems certain from this that the quantity of tannic acid, roughly estimated to be in the Spurge-extract, is much less than the real quantity, or it may be that the other components of the extract play a more important part than has been credited to them.

Some mention should be made of the peculiar phenomenon that the

trout in its earliest post-larval stages is comparatively immune from the action of both Spurge-extract and tannic acid. Very strong solutions of both had to be employed before fatal effects were produced, and even then the time taken was much greater than for older specimens in weaker solutions. At later stages the larvæ gradually lost this power of resisting the action of the Spurge and tannin.

The time taken by the Spurge to produce fatal effects varies, of course, with the strength of solution employed. In the 'strongest possible extract death would occur in a few seconds. In a 20 per cent. solution of the fresh extract prepared as previously described death takes place within five minutes. As the solutions grow weaker the time taken becomes longer until with a solution of 0.01 per cent 4 hours elapse ere death occurs. The time varies, it should be said, with different specimens, but these represent the averages. The 0.01 per cent. solution is the weakest that need be considered for all practical purposes. This is 1 part in 10,000, and shows that a pool 100 feet long by 20 feet broad and 5 feet deep would prove fatal to all fishes within 4 hours if 1 cubic foot or 6 gallons of the fresh extract were poured into it. If, however, the plants are cut up, pounded, and placed directly into the pool, then a much smaller quantity would suffice. For, as has been previously stated, the "fresh extract" does not exhaust the possibilities of the plant, and several hours may elapse ere the poison is entirely dissolved out of it. The calculation is somewhat rough, but if we take an entire plant when fully developed to weigh about 400 grammes, then about a hundred plants are needed to poison a pool of the dimensions given. If the plants are pounded and placed in the pool, however, probably a fifth of this number would suffice.

If such a pool were almost stagnant, with little water passing through, it would be fatal to fishes, not merely for hours but days.

Reference to Table I will show that the Spurge-extract retains its deadly qualities for several days, and if the quantity thrown into the pool be not less than that quoted above, the fish there have little chance of escaping death. If the water be running in and out of the pool, the same effects will result from placing the plants at its upper end, for their presence there will keep the pool in a poisoned state for many hours and even a whole day. It is evident therefore that the salmon which lie in quiet pools waiting their opportunity to get up the rivers, are especially liable to be killed in this way. If they are swimming about in a broad reach of water they will be unaffected by any small current containing the Spurge-extract—unless it be in enormous quantity. But the peculiarity of the poison, causing as it does a loss of sensibility and consequent stupidity, affects the resting fish in such a way that it comes under the influence of the more fatal component of the Spurge before it is able to detect anything

wrong in the water. And once the gills are affected, there is little chance of the fish escaping. The whole habits of the salmon, in short, render it peculiarly liable to this form of poisoning.

*Summary.*

Chemical analysis of the Spurge-extract shows that it contains tannic acid. Experiments on the circulation in the lung and mesentery of the frog reveal a close similarity between the action of the Spurge-extract and of tannic acid. In the case of trout the similarity extends to the non-recovery of the fish in fresh water, after they have come under the influence of either Spurge-extract or tannic acid. The power of the Spurge-extract to produce fatal effects persists for several days without diminution. Twenty per cent. of the fresh extract is fatal within 5 minutes, whilst 0.01 per cent. takes 4 to 6 hours, and seems to be the smallest percentage which has fatal results. In the case of fishes, death is considered to ensue from the inflammation of the gills and consequent stasis of the circulation, set up by the action of the tannic-acid component of the Spurge-extract. The fresh extract is calculated roughly to contain about 1 per cent. of tannic acid, but on this estimation the Spurge-extract is fatal within a shorter period than the corresponding quantity of tannic acid. Hence, the percentage of tannic acid has been under-estimated, or some other substance or substances in the extract also aid in producing fatal effects.

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“On Chemical Dynamics and Statics under the Action of Light.”

By MEYER WILDERMAN, Ph.D., B.Sc. (Oxon.). Communicated by Dr. LUDWIG MOND, F.R.S. Received January 30,—  
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(Abstract.)

Since the second half of the last century chemical statics and dynamics have developed into a veritable science of their own. The general law governing velocity of chemical reaction and chemical equilibrium in homogeneous systems is now known as the law of action of mass;\* the law governing velocity of physical or molecular transformations in heterogeneous systems proves also to be of a general and simple nature: the velocity is directly proportional to the surface of contact of the reacting parts and to the remoteness of the system from the point of equilibrium;† the velocity of chemical

\* Wilhelmy, Harcourt and Esson, Guldberg and Waage, Van't Hoff.

† M. Wilderman, ‘*Zeitschrift für Physikalische Chemie*,’ 1899, and especially ‘*Phil. Mag.*,’ July, 1901.